UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/064,057	04/22/1998	GARY F. GERARD	0942.4330002	5386

26111 7590 05/07/2002

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W., SUITE 600
WASHINGTON, DC 20005-3934

EXAMINER	
NASHED, NASHAAT T	

ART UNIT	PAPER NUMBER
1652	4

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/064,057	Applicant(s) Gerard et al.
	Examiner Nashaat T. Nashed	Art Unit 1652

-- The MAILING DATE of this communication appears on th cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 20, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *26, 28, 33, 39, 40, 117-125, and 127-148* is/are pending in the application.

4a) Of the above, claim(s) *39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *26, 28, 33, 40, 117-125, and 127-148* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 20, 2002 has been entered.

The application has been amended as requested in the communication filed Febraury 20, 2002. Accordingly, claims 34, 37, and 126 have been canceled, claims 26, 28, 33, 117-121, 124, 125, and 127-135 have been amended, and claims 136-148 have been entered.

Claims 26, 28, 33, 39, 40, 117-125, and 127-148 are pending and under consideration in this Office action.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

Groups I-XI Claims 26, 28, 33, 39, 40, 117-125, and 127-148, drawn to method of making Avian Sarcoma-Leukosis Virus (ASLV) reverse transcriptases which encompases at least 11 independent enzymes, classified in Class 435, subclass 194.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I-XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions are drawn to independent method of making idependent chemical entities with different physical and chemical properties.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Groups II-XI, restriction for examination purposes as indicated is proper.

During a telephone conversation with Robert W. Esmond on April 19, 2002 a provisional election was made with traverse to prosecute the invention of Group I, AMV reverse transcriptase, claims 26, 28, 33, 40, 117-125, and 127-148. Affirmation of this election must be made by applicant in responding to this Office action. Claims 39 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the application disclouses several reverse transcriptases from several viruses and methods of their making as well as method of making mutents thereof. Neither the nucleic and/or amino acid sequences are found in the specification. The specification reference specific amino acid residues from supositly an amino acid sequence without identifying the amino acid sequence with a sequence identification number, see for example page 57, lines 11 and 12. Another sequence on page 73, line 22, is not accompanied by a sequence identification number. The previously mention non-compliance with the sequence rule are intended to be an examples and not as an exhustive list of non-compliance with the sequence rules. Applicants are required to bring their application to full compliance with the sequence rules.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Recombinant Method for Making AMV-Reverse Transcripatese and Mutant Thereof.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 26, 28, 33, 117-125, and 127-148 are objected to because they contain non-elected subject matter.

Claims 26, 28, 33, 117-125, and 127-148 are objected to under 37 CFR § 1.75(d)(1) as being in improper form because the claim states an improper Markush groups. Compounds included within a Markush group must "(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." (See MPEP § 803.02.) The specification defines the abriviation ASLV reverse transcriptase as any reverse transcriptase from any one of the viruses listed on page 4, lines 1-10, which defines a Markush group. The various members of the Markush group in the claims are different chemical compound and do not share a common structural feature required for the stated utility, i. e., the reverse transcriptase activity.

Claim 33, 40, and 127-147 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 33 and 40 are dependent on claim 26. Since the phrase "ASLV reverse transcriptase", is assumed to mean AMV-reverse transcriptase, see the rejections made under 35 U. S. C. §112, second paragraph, the claims do not further limit claim 26. Similarly, the phrase "units per milligram" is assumed to mean any reverse transcriptase activity.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 28, 33, 117-125, and 127-148 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 26, 28, 33, 40, 117-125, and 127-148 are directed to a recombinant method of making retroviral transcriptases and their mutants which have RNase activity and having at lease 30,000 units per milligram and mutants thaereof. The specification, however, fails to provide an adequate written description of the claimed invention. No structure for the nucleic and/or the amino acid sequences for the AMV-reverse transcriptase and enzymatically active mutants thereof, or the source of the genomic RNA are disclosed. Also, the

specification fails to define a unit of activity. In addition, applicants failed to teach a preparation of any AMV-revese transcriptase having any kind of activity. Finaly, it appears that the applicants is attempting to claim hybrid reverse transcriptase formed from various subunits from the different species of ASLV. The specification does not teach such a hybid or how to make or even attribute a transcriptase activity from a heterologus dimer formed from α- and/or β-subunits from different species of the ASLV's. Given this lack of written description, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 26, 28, 33, 40, 117-125 and 127-148 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) claims 26, 28, 33, 40, 117-125 and 127-148 contain the undefined abbreviations ASLV and AMV. Abbreviations and acronyms must be defined at least once in the claims.

(b) Claim 26 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is a purification of the reverse transcriptase from the culture of the host cell, after step (b) and before step (c).

(c) the phrases "ASLV reverse transcriptase" in claims 26, 28, 33, 40, 117-125 and 127-148; "specific activity ..... units per milligram" in claims 26, and 127-147, and "one or more subunits" in claims 28, and 117-120 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. It is noted that ASLV, presumably, Avian Sarcoma-Leukosis Virus, reverse transcriptase is definded in the specification starting on last two lines on page 3, through line 6 on page 4, but the definition contains the clouse "which includes but not limited to ...." that renders the claim indefinit. The specification and the claims do not define the activity or a unit of activity. Reverse transcriptases are multifunctional enzymes, and known to have several activities that include RNA-directed DNA-polymerase, DNA-directed DNA-polymerase and RNase H activity. Since one of ordinary skill in the art would not know which one of said specific activities the claims are refereing to and the meaning of unit of activity, the ordinary skilled in the art would not know the metes and bounds of the claimed invention. One or more subunit is considered indefinit because the enzymatically active form of the enzyme is a dimer and therefore there could not be more than two subunits per molecule of enzyme. For examination purposes: (i) ASLV reverse transcriptase is assumed to be

AMV-reverse transcriptase; (ii) specif activity ..... units per milligram is assumed to mean enzymatically active preparation, and (iii) "one or more subunits" is assumed to mean homa dimer containing two α-AMV reverse transcriptase or two β-AMV reverse transcriptase; or heterodimer containig one of each the α- and β-subunits of AMV reverse transcriptase.

(d) the phrase "having RNase H activity" in claim 26 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The phrase in light of the specification has more than one meaning. The first is a wild-type RNase activity, whereas the second could mean having reduced RNase activity relative to that of the wild-type. For examination purposes only, the phrase is taken to mean having any degree of RNase activity including that of the wild-type AMV-reverse transcriptase.

(e) the phrases "one or more ASLV reverse transcriptase" in claim 28, 117, 121, and 148 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. For examination purposes, the phrase is assumed to enzymatically active mutants of AMV-reverse transcriptase.

(f) the phrase "βp4 subunit" in claim 28, 120, and 148 is not structurally defined by the specification or the claim, and therefore, the claim is considered indefinit. For examination purposes, the phrase is interpeted as a mutant or naturally occuring allilic variants of the β-subunit which has a reverse transcriptase activity.

(g) All other claims not mentioned in (a)-(f) are included in these rejection because they are dependent from rejected claims and do not correct their deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26, 28, 33, 40, 117-119, 121-125 and 127-148 are rejected under 35 U.S.C. § 102(b) as being anticipated by Soltis *et al.* (see IDS: Proc. Natl. Acad. Sci. U. S. A. **1988**, 85, 3372-3376).

Soltis *et al.* teach the expression separtly of both the α- and β-subunits of AMV-reverse transcriptase in *E. coli* host cell. They teach that the isolated α- and β-subunits

have a reverse transcriptase and function as homodimers, see abstract. They teach the construction of pRC23-p95 for α-subunit and pRC23-p63 for β-subunit, see page 3372, ridht column, last two paragraphs, the purification and assay for the enzyme, see page 3373, right column (claims 26, 28, 33, 40, 117-122, 124, 125, 127-148). Although applicant had previously argued similar rejection on the record successfully, this rejection is reinstated because the unit and type of activity is not defined in the specifcation and/or the claims. Since the claims are being interpeted as having any enzymatic activity of any one of the known activities of AMV-reverse transcriptase, the reference anticipate the claimed invention.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 26, 28, 33, 40, 117-119, 121-125 and 127-148 are rejected under 35 U.S.C. § 103 as being unpatentable over Soltis *et al.* in view of the state of the art at the time of the application was filed.

The teaching of Soltis *et al.* are summerized above.

AMV-reverse transcriptase has been used extensively in biotechnology in the preparation of cDNA libraries. Thus, one of ordinary skill in the art would have had motivation at the time of invention to produce AMV-reverse transcriptase by a recombinant method. Thus, the ordinary skill in the art would have constructed a vector(s) comprising a nucleic acid sequence encoding the α- and β-subunits of AMV-reverse transcriptase, transform a host cell with said vector(s) and culture the host cell as taught by Solties, and purify the enzyme to any specific activity that suits his/here purposes, i. e., to any specific activity of any desired activity, by well known methods in the prior art (claim 26, 28, 33, 40, 117-119, 121, 122, and 127-148). Also, the ordinary skill in the art would have been further motivated to coexpress the α- and β-subunits in the same host cell to produce the heterodimer because the heterodimer have higher thermalstability, see the abstract of Soltis *et al.* Thus, the ordinary skill in the art would have constructed the pRC23-p95 and pRC23-p63 taught by Soltis and coexpress them in a single host cell to produce the heterodimer (claim 123 and 125). In addition, one of ordinary skill in the art would be further motivated to construct a single vector comprising the coding sequences for both the α- and β-subunits of AMV-reverse transcriptase under the control of the same promoter which would lead to the production of equal amount of the two subunits (claim 124). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner